In the Claims

Please amend the claims as follows. The claims listed below are intended to reflect amendment of claims 33 and 50. Support for the amendments to the claims is found in the claims as originally filed, and within the specification.

1. (Canceled). A method of identifying a therapeutic agent, which decreases the presence of double minute chromosomes or extrachromosomal DNA in a cell, comprising:

contacting a portion of test cells with a potential therapeutic agent to produce treated test cells wherein the test cells contain a known level of double minute chromosomes or extrachromosomal DNA and are capable of undergoing micronucleation; and

assaying the treated test cells to determine their level of micronucleation of double minute chromosomes or extrachromosomal DNA, wherein an increased level of micronucleation and decreased level of double minute chromosomes or extrachromosomal DNA relative to that of an untreated portion of test cells indicates that the potential therapeutic agent is an actual therapeutic agent.

2. (Canceled) The method of claim 1, wherein the test cells lack functional tumor suppressor protein.

3. (Canceled) The method of claim 1, wherein the test cells contain an oncogene.

4. (Canceled) The method of claim 1, wherein assaying is conducted by FISH, flow cytometry, centrifugal fractionization or histone-GFP labeling.

5. (Withdrawn) A therapeutic agent identified by the method of claim 1.

6. (Withdrawn) A method for inducing maturation or death of a suitable cell, the method comprising contacting the suitable cell with an agent that induces or enhances elimination of DM or extrachromosomal DNA from the suitable cell by micronucleation.

7. (Withdrawn) The method of claim 6, wherein the cell lacks functional tumor suppressor protein.

8. (Withdrawn) The method of claim 6, wherein the suitable cell contains an amplified oncogene.

9. (Withdrawn) The method of claim 6, wherein the suitable cells are contacted in vitro, ex vivo or in vivo.

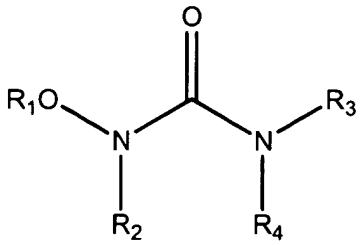
10. (Withdrawn) A method of treating a subject with a disease relates to the presence in the subject of cells containing DM or extrachromosomal DNA and the capacity to eliminate DM or DNA by extra micronucleation, the method comprising administering to the subject an effective amount of an agent that induces or enhances elimination of DM or extra chromosomal DNA by micronucleation from the cells.

11. (Withdrawn) The method of claim 10, wherein the cells lack a functional tumor suppressor protein.

12. (Withdrawn) The method of claim 10, wherein the cells contain an amplified oncogene.

13. (Withdrawn) The method of claim 10, wherein the agent is hydroxyurea or a derivative thereof.

14. (Withdrawn) The method of claim 6 or 10, wherein the agent is a compound having the formula:



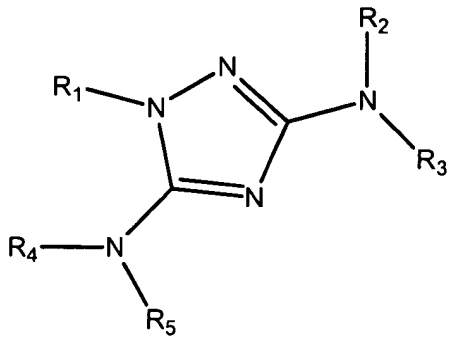
wherein R1 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyl or -(CH2)n-X, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of halo, -OH, -NR2, -OR, -C(O)OR, -OC(O)R, amide and acyl wherein R is H, alkyl or aryl;

R2 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, C(O)R' or -(CH2)n-X, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and wherein R' is alkyl or aryl and substiuents are as defined above;

R3 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, OR", NR"2 or -(CH2)n-X, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of-OH, NR"2, -OR", -C(O)OR", -OC(O)R", amide and acyl wherein R" is H, alkyl or aryl; and

R4 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, or (CH2)n-X, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of -OH, -NR"'2, OR"', -C(O)OR"', -OC(O)R"', amide and acyl wherein R"' is H, alkyl or aryl.

15. (Withdrawn) The method of claim 6 or 10, wherein the agent is a compound having the formula:



wherein R1 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyl or-(CH2)n-X, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of halo, -OH, -NR2, -OR, -C(O)OR, -OC(O)R, amide and acyl wherein R is H, alkyl or aryl;

R2 and R4 are independently H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, OR', NR'2 or -(CH2)n-X, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of-OH, -NR'2, -OR', -C(O)OR', -OC(O)R', amide and acyl wherein R' is H, alkyl or aryl; and

R3 and R5 are independently H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl or -(CH2)n-X, wherein n is an integer from 1 to 4, n is an integer from I to 4; X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of-OH, -NR"2, -OR", -C(O)OR", OC(O)R", amide and acyl wherein R" is H, alkyl or aryl.

16. (Withdrawn) A method of detecting DM or extrachromosomal DNA in a cell, the method comprising the steps of:

introducing into the cell a detectably labeled protein, wherein the protein specifically associates with DM and extrachromosomal DNA in the cell; and

detecting the complex of labeled protein and/or DM or extrachromosomal DNA thereby indicating the pressure of DM and extrachromosomal DNA in the cell.

17. (Withdrawn) The method of claim 16, wherein the protein is histone or an analog thereof.

18. (Withdrawn) The method of claim 16, wherein the detectable label is a fluorescent label.

19. (Withdrawn) The method of claim 18, wherein the fluorescent label is Aequorea victoria green fluorescent protein, Aequorea victoria cayenne fluorescent protein or Aequorea victoria yellow fluorescent protein.

20. (Withdrawn) The method of claim 16 wherein the labeled protein is introduced into the cell by contacting the cell with a vector comprising a DNA encoding detectably labeled histone fusion protein.

21. (Withdrawn) The method of claim 20 wherein the histone fusion protein is H2B-GFP.

22. (Withdrawn) The method of claim 20, wherein the vector is a retroviral vector.

23. (Withdrawn) A method for monitoring the movement of chromosomal DNA material in a cell, comprising:
introducing into the cell a detectably labeled protein, wherein the protein specifically associates with chromosomal DNA in the cell to provide a labeled complex;
detecting labeled complex thereby detecting chromosomal DNA in the cell; and
comparing the location of the labeled complex with uncomplexed chromosome.

24. (Withdrawn) The method of claim 23, wherein the protein that specifically associates with the chromosomal DNA in the cell is centromere binding protein or lac operator.

25. (Withdrawn) The method of claim 23, wherein the movement of the chromosome is selected from the group consisting of chromosome condensation, chromosome decondensation, nucleolar formation, heterochromatin movement, chromosome fragmentation, chromosome bridge formation, micronucleation, gene amplification, formation of aneuploidy, chromosome loss and chromosome translocation.

26. (Withdrawn) A method of detecting a pathological cell phenotype, the method comprising:

introducing into the cell a detectably labeled protein, wherein the protein specifically associates with DM and extrachromosomal DNA to provide a labeled complex;

detecting the labeled complex, thereby detecting DM and extrachromosomal DNA associated with the pathological phenotype; and

comparing the pathological phenotype with the phenotype of a reference cell.

27. (Withdrawn) The method of claim 26, wherein the pathological phenotype is cancer or a neoplastic disease.

28. (Canceled) A method according to claim 1 comprising determining whether the treated test cells have undergone reversion of a neoplastic phenotype, differentiation or apoptosis.

29. (Canceled) A method of identifying a therapeutic agent suitable for treatment of neoplastic cells having double minute chromosomes or extrachromosomal DNA, comprising:

contacting test cells with a potential therapeutic agent to produce treated test cells wherein the test cells contain double minute chromosomes or extrachromosomal DNA, are neoplastic and are capable of undergoing micronucleation; and

assaying the treated test cells to determine their level of micronucleation of double minute chromosomes or extrachromosomal DNA, wherein an increased level of micronucleation relative to that of an untreated portion of test cells indicates that the potential therapeutic agent is an actual therapeutic agent.

30. (Canceled) A method according to claim 29 comprising determining whether the treated test cells have undergone reversion of a neoplastic phenotype, differentiation or apoptosis.

31. (Withdrawn) A method for identifying a therapeutic agent suitable for treatment of neoplastic disease in a patient, comprising:

administering a potential therapeutic agent of an animal carrying neoplastic cells having double minute chromosomes or extrachromosomal DNA and being capable of undergoing micronucleation, and

examining the animal to determine whether the quantity of neoplastic cells has been lessened.

32. (Withdrawn) A method according to claim 31 wherein the examination is made by determining whether the neoplastic cells of the animal receiving the potential therapeutic agent have undergone more reversion, apoptosis or cell differentiation relative to the reversion, apoptosis or cell differentiation of neoplastic cells of an untreated animal control.

33. (Amended) A method to identify an agent that increases or decreases the amount of double minute chromosomes or extrachromosomal DNA in a cell, comprising contacting the cell with the agent, wherein the cell expresses a labeled protein that associates with double minute chromosomes or extrachromosomal ~~extracellular~~ DNA to form a labeled complex; and comparing the amount of the labeled complex contained in the cell contacted with the agent with the amount of labeled complex contained in a cell that was not contacted with the agent.

34. (Previously Added) The method of claim 33, wherein the cell is alive when the amount of labeled complex is compared.

35. (Previously Added) The method of claim 33, wherein the cell is dead when the amount of labeled complex is compared.

36. (Previously Added) The method of claim 33, wherein the labeled protein comprises a fluorescently labeled protein.

37. (Previously Added) The method of claim 33, wherein the labeled protein is a fluorescent protein fused to a protein that associates with DNA.

38. (Previously Added) The method of claim 37, wherein the fluorescent protein is Aequorea victoria green fluorescent protein, Aequorea victoria cayenne fluorescent protein or Aequorea victoria yellow fluorescent protein.

39. (Previously Added) The method of claim 33, wherein the labeled protein that associates with DNA is a histone or an analog thereof.

40. (Previously Added) The method of claim 39, wherein the histone is H3, H4, H2A or H2B.

41. (Previously Added) The method of claim 39, wherein the histone is H2B.

42. (Previously Added) The method of claim 33, wherein the cell contains an oncogene.

43. (Previously Added) The method of claim 33, wherein the cell lacks at least one functional tumor suppressor gene.

44. (Previously Added) The method of claim 33, wherein the cell expresses a non-functional p53 protein.

45. (Previously Added) The method of claim 33, wherein the cell is a cancer cell.

46. (Previously Added) The method of claim 33, wherein the cell is a human cell.

47. (Previously Added) The method of claim 33, wherein the cell is a neoplastic cell.

48. (Previously Added) The method of claim 33, wherein the labeled complex is compared with fluorescence microscopy or flow cytometry.

49. (Previously Added) The method of claim 33, further comprising determining if the cell has undergone reversion of a neoplastic phenotype, differentiation or apoptosis.

50. (Amended) The method of claim 33 ~~A method to identify an agent that increases or decreases the amount of an extrachromosomal DNA in a cell, comprising contacting the cell with the agent~~, wherein the ~~cell expresses a~~ labeled protein ~~that~~ is a non-centromere binding protein or a lac repressor ~~operator that associates with the extrachromosomal DNA to form a labeled complex; and comparing the amount of the labeled complex contained in the cell contacted with the agent with the amount of labeled complex contained in a cell that was not contacted with the agent~~.

51. (Canceled) A therapeutic agent identified according to the method of claim 33.

52. (Canceled) A therapeutic agent identified according to the method of claim 50.

53. (Previously Added) The method of claim 33, wherein the comparing is done in vitro, in vivo or ex vivo.

54. (Previously Added) The method of claim 50, wherein the comparing is done in vitro, in vivo or ex vivo.